BRITISH PHARMACOLOGICAL SOCIETY

Today's science, tomorrow's medicines

British Pharmacological Society response to the Welsh Government's review of the appraisal of orphan and ultra-orphan medicines in Wales

1. The British Pharmacological Society (BPS) welcomes the review's consideration of scientific rigour, inclusiveness, transparency, independence, challenge and review, support for implementation, timeliness, consistency, connectivity and equity in drawing its recommendations for the appraisal of treatments for rare diseases in Wales.
2. *Distinction should also be made between orphan and conventional medicines*. Applying the same appraisal criteria to orphan drugs that are not ultra-orphan (hereafter referred to as orphan drugs) as to ultra-orphan drugs may be problematic if the case for preferential funding has not been made for orphan drugs. The review acknowledges that previous research has indicated that there may be a case for having different appraisal and assessment systems for ultra-orphan drugs, but that the case is weaker for orphan drugs. Reference is made to population surveys that do not lend support to the view that premium prices should be paid for rarity. Additional relevant evidence comes from research which solicited All Wales Medicines Strategy Group (AWMSG) and the New Medicines Group members' (n=41) views on appraisal criteria that deviate from the reference case[1]. Appraisal committee members expressed a view of indifference, with a median score of 3 (on a Likert scale of 1=strongly disagree to 5=strongly agree), that all else being equal, the NHS should be prepared to pay a premium for medicines that are intended for the treatment of very rare diseases (IQR 3, 4; Range 1, 5). Applying the same appraisal criteria to orphan drugs as to ultra-orphan drugs will also lead to differences in how the AWMSG and NICE appraise medicines (NICE applies the same appraisal criteria to orphan drugs as it does to non-orphan drugs), given that an alignment in processes has hitherto been an important consideration for the AWMSG. Moreover it is unclear whether the NHS in Wales should adopt NICE's Highly Specialised Technologies evaluations, which will include ultra-orphan drugs, or whether the proposed orphan/ultra-orphan Medicine Group subsumes this activity.
3. *There should not be a separate fund for orphan and ultra-orphan medicines*. BPS supports the view that a separate, ring-fenced fund for

[1] Linley WG, Hughes DA. Decision-makers' preferences for approving new medicines in Wales: a discrete-choice experiment with assessment of external validity. Pharmacoeconomics. 2013 Apr;31(4):345-55.

orphan and ultra-orphan drugs in Wales would increase inequities in care. Not having a fund for orphan and ultra-orphan medicines is consistent with Wales not having a cancer drugs fund.

4. *Involvement with key stakeholders at all stages during the appraisal process*. BPS agrees that stakeholder engagement is important in all health technology appraisals, and involvement of specialist organisations (e.g. WHSSC) should be prioritised.
5. *An orphan/ultra-orphan Medicine Group should be established in parallel with the New Medicines Group (NMG)*. Notwithstanding BPS' view on making no distinction between orphan drugs and ultra-orphan drugs, the recommendation for a separate appraisal group might lead to inconsistencies in the application of appraisal criteria compared to other medicines. This could be mitigated by ensuring a broad representation from the NMG on the orphan/ultra-orphan Medicine Group, and for the AWMSG to continue its role as the parent committee in relation to the appraisal of these treatments.
6. *The role of WHSCC should be amended to enable closer involvement and integration with the appraisal process*. Since its establishment in 2002, the AWMSG has significantly improved the processes by which new medicines are introduced to the NHS in Wales. This has led to clinically effective and cost-effective treatments being made available to patients in a timely and equitable manner. The review's recommendations for further improvements, through closer collaboration with WHSSC and links to the IPFR process, are welcomed.
7. *The QALY as a common currency to gauge the relative cost-effectiveness of medicines in securing patient benefit across therapeutic areas, should also apply to the appraisal of orphan and ultra-orphan medicines*. The BPS strongly supports the use of the QALY and the cost-per-QALY measure for the assessment and appraisal of all medicines. Accepted methods for their calculation should be used, including patient (and carers) generated utility values wherever possible.
8. *A system for on-going monitoring and evaluation must be established. Whenever possible, stopping criteria for orphan or ultra-orphan medicines need to be agreed and rigorously enforced*. As with all medicines, applying appropriate stopping rules where there is no response or when toxicity occurs is key to achieving the greatest benefits in a cost-effective manner.
9. *A wider societal perspective should be encompassed in the criteria employed in the appraisal process for orphan and ultra-orphan medicines*. The AWMSG already considers broader societal impact in appraising all medicines: "AWMSG will consider whether the medicine has an impact on non-health benefits that are not captured in the quality-adjusted life year (QALY) (e.g. impact on families and carers, work and schooling), costs to sectors outside the NHS / PSS such as educational services, and productivity losses attributable to changes in health outcomes." How this should be different for orphan and ultra-orphan drugs in unclear. Evidence supporting broader societal preferences towards the funding of treatments for rare diseases is weak.
10. *The value frameworks offered by the OHE and AGNSS represent useful approaches that should be considered further*. BPS is cautious of the recommendation to consider the use of multi criteria decision analysis. This is an untested method in the context of HTA in the UK, and a method

which might not appropriately capture the opportunity cost associated with positive recommendations for cost-incurring medicines.

11. *QALYs should be weighted along the lines of AWMSG/NICE end-of-life procedures to reflect societal perspectives*. The BPS strongly recommends that further research should be commissioned to determine the magnitude of these weights, so that societal preferences for the treatment of rare diseases are reflected appropriately.
12. *Value for money considerations should take into account the cost difference between orphan or ultra-orphan medicines and conventional medicines whilst reflecting on the clinical context and opportunity costs*. This is aligned with the use of the QALY which provides a common metric for the consideration of the different clinical context and of the opportunity cost.
13. BPS supports each of the review's recommendations in relation to equity.

About the British Pharmacological Society

The British Pharmacological Society (BPS) is the primary UK learned society concerned with research into drugs and the way they work. Our members work in academia, industry, regulatory agencies and the health services, and many are medically qualified. The Society covers the whole spectrum of pharmacology, including laboratory, clinical, and toxicological aspects.

Clinical pharmacology is the medical speciality dedicated to promoting safe and effective use of medicines for patient benefit. Clinical pharmacologists work as consultants in the NHS and many hold prominent positions in UK Universities.